TITLE: Preparation of pyrimidine derivatives as NK1 antagonists
INVENTOR(S): Stadler, Heinz
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042280	A2	20020530	WO 2001-EP13084	20011113 <--
WO 2002042280	A3	20020822		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001015480	A	20031021	BR 2001-15480	20011113 <--
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IN 2003CN00786	A	20050415	IN 2003-CN786	20030521 <--
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PRIORITY APPLN. INFO.: EP 2000-125529 A 20001122 <--
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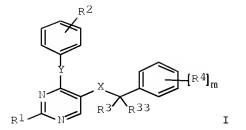
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 137:6189
ED Entered STN: 31 May 2002
GI



I

AB The title compds. [I; R1 = alkyl, alkoxy, pyridinyl, pyrimidinyl, etc.; R2 = H, alkyl, alkoxy, halo, CF3; R3, R33 = H, alkyl; R4 = halo, CF3, alkoxy; R5 = H, alkyl; X = CONR, NRCO; Y = O, S, SO2, NR; m = 0-2] which have a good affinity to the NK1 receptor and therefore are suitable in the treatment of diseases, related to this receptor, were prepared and formulated. Thus, reacting 4-chloro-2-methylsulfanylpyrimidine-5- carboxylic acid Et ester with o-cresol in the presence of Cs2CO3 in MeCN (99%) followed by saponification (47%), and amidation of the resulting acid with [3,5-bis(trifluoromethyl)benzyl]methylamine (96%) afforded I [R1 = SMe; R2 = 2-Me; R3, R33 = H; R4 = 3,5-(CF3)2; Y = O; X = CONMe] which showed pKi of 7.38 against NK-1 receptor binding.

IC ICM C07D239-56
ICS C07D239-46; C07D239-52; A61K031-505; A61P025-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 432520-79-1P 432520-80-4P 432520-81-5P 432520-82-6P 432520-83-7P
432520-84-8P 432520-85-9P 432520-87-1P 432520-88-2P 432520-89-3P
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432521-05-6P 432521-06-7P 432521-07-8P 432521-08-9P 432521-09-0P
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432521-38-5P 432521-39-6P 432521-41-0P 432521-42-1P 432521-43-2P
432521-44-3P 432521-45-4P 432521-46-5P 432521-47-6P 432521-48-7P
432521-49-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidine derivs. as NK1 antagonists)

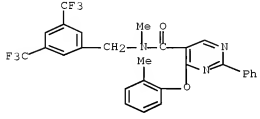
IT 75-65-0, tert-Butanol, reactions 87-13-8, Diethyl ethoxymethylenemalonate 95-48-7, o-Cresol, reactions 108-00-9, 2-Dimethylaminoethylamine 108-01-0, 2-Dimethylaminoethanol 109-01-3, 1-Methylpiperazine 110-85-0, Piperazine, reactions 110-91-8, Morpholine, reactions 123-90-0, Thiomorpholine 622-40-2, N-(2-Hydroxyethyl)morpholine 5909-24-0, 4-Chloro-2-methanesulfanylpyrimidine-5-carboxylic acid ethyl ester 15400-46-1 15521-18-3, 2-Dimethylaminopropanol 39989-43-0, 3,5-Dichlorobenzylamine 56406-44-1 77775-71-4 138588-40-6 148452-35-1 159820-24-3 289686-69-7 432521-64-7 432521-65-8 432521-66-9 432521-67-0 432521-68-1 432521-69-2 432521-70-5 432521-71-6 432521-72-7 432521-73-8
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyrimidine derivs. as NK1 antagonists)

IT 432521-18-1P 432521-49-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidine derivs. as NK1 antagonists)

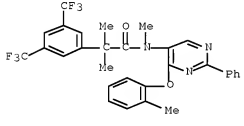
RN 432521-18-1 HCAPLUS

CN 5-Pyrimidinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenoxy)-2-phenyl- (CA INDEX NAME)



RN 432521-49-8 HCAPLUS

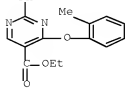
CN Benzeneacetamide, N,α,α-trimethyl-N-[4-(2-methylphenoxy)-2-phenyl-5-pyrimidinyl]-3,5-bis(trifluoromethyl)- (CA INDEX NAME)



IT 432521-69-2 432521-73-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrimidine derivs. as NK1 antagonists)

RN 432521-69-2 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-(2-methylphenoxy)-2-phenyl-, ethyl ester (CA INDEX NAME)



RN 432521-73-8 HCAPLUS
CN 5-Pyrimidinamine, N-methyl-4-(2-methylphenoxy)-2-phenyl- (CA INDEX NAME)